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|---|---|
| TRAN, MY CHAU T | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1639 | |

DATE MAILED: 10/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/835,096. | SHORT, JAY M. | |
| | Examiner | Art Unit | |
| | MY-CHAU T TRAN | 1639 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *06 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-50 and 60-93* is/are pending in the application.

4a) Of the above claim(s) *2,8,10,18,19,24,27,29-31,35-39,49,50 and 60-84* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-7,9,11-17,20-23,25,26,28,32-34,40-48 and 85-93* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 April 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/18/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Status of Claims*

1. Applicant's amendment filed 8/15/2003 is acknowledged and entered. Claims 51-59 have been canceled. Claims 85-93 have been added.

2. Claims 1-50, and 60-93 are pending.

### *Election/Restrictions*

3. Applicant's election with traverse of Group 1 (Claims 1, 3-26, 28-29, 31-48, and 77) in the reply filed on 8/15/2003 is acknowledged.

The traversal is on the ground that Group 4 (Claim 50) be rejoined with Group 1 because it would not be an undue burden to search Group 4, which includes additional steps related to separating and combining scaffolding components using sexual PCR, with Group 1.

This is not found persuasive because the method of Group 4 is distinct from the method of Group 1. The product, i.e. the set of morphatides, of Group 4 is structurally distinct, i.e. the steps of separating and combining scaffolding components using sexual PCR generate new scaffolding components that produce another set of morphatides, i.e. different morphatides, from the product, i.e. the set of morphatides, of Group 1. Thus the method of Group 4 is distinct from the method of Group 1 and Group 4 is not rejoined with Group 1.

The requirement is still deemed proper and is therefore made FINAL.

4. Claims 2, 27, 30, 49-50, 60-76, 78-84 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to ***nonelected inventions***, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 8/15/2003.

5. Applicant has elected with traversed the following species for the elected invention (Claims 1, 3-26, 28-29, 31-48, 77 and new claims 85-93) in the reply filed on 8/15/2003 and 7/6/2004:

a. A single specific species of a scaffold. Applicant elected the nucleic acid scaffold having a 5' and 3' flanking region with a sequence as set forth in SEQ ID Nos. 1 and 2 and a randomized middle sequence of 36 nucleotides that includes 3 of the 4 bases occurring at similar frequency and one of the four bases occurring at a rare frequency of 5% (i.e. 2 positions).

b. A single specific species of "linker" and number of "linkers". Applicant elected two identical linkers that are formed by reacting phenylboronic acid with salicylhydroxamic acid, each linker being bound to a uridine residue on the scaffold through a 5-position of a uracil base of the uridine residue.

c. A single specific species of "agent" and number of "agent". Applicant elected two threonine residues each bound to a linker through a carboxyl group on each of the threonine molecules.

d. A single specific species of target. Applicant elected a thrombin target.

e. A single specific mode of interaction with the target. Applicant elected the interaction is a morphatide that binds to, or associates with an agent.

f. A single specific mode of separating the "morphatide". Applicant elected the method of separation is chromatography.

Applicant's traversal of the species election is on the ground that the recited species of morphatides have identical operation, function, and effect in the presently claimed method and thus should not be restricted.

This is not found persuasive because the morphatides claimed in the presently claimed method recites patentably distinct species of morphatides that differ in operation, function, and effect. The morphatides claimed in the presently claimed method encompasses "one or more complexes", i.e. complexes of the presently claimed morphatides do not exclude complexes that are not identical operation, function, and effect. Thus claimed morphatides of the presently claimed method recites patentably distinct species of morphatides that differ in operation, function, and effect.

The requirement is still deemed proper and is therefore made FINAL.

6. Claims 8, 10, 18-19, 24, 29, 31, 35-39, and 77 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to ***nonelected species***, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 8/15/2003 and 7/6/2004.

***Priority***

7. This application is CON of 08/953,634 filed 10/17/1997, which is a CIP of 08/839,468 filed 4/14/1997. Application of 08/839,468 claims priority to a provisional application 60/028,527 filed 10/17/1996.

***Information Disclosure Statement***

8. The information disclosure statements (IDS) submitted by applicant filed on 7/18/2003 is acknowledged and considered as noted on PTO-1449.

9. Claims 1, 3-7, 9, 11-17, 20-23, 25-26, 28, 32-34, 40-48, and 85-93 are treated on the merit in this Office Action.

10. Please note: Applicant's *specifically* elected species, i.e. morphatides (see response dated 7/6/2004, figure/drawing; also paragraph 5 above) was searched and was not found in the prior art. Also, see MPEP § 803.02 (emphasis added):

> On the other hand, should no prior art be found that anticipates or renders obvious the elected species, the search of the Markush-type claim will be extended. If prior art is then found that anticipates or renders obvious the Markush-type claim with respect to a nonelected species, the Markush-type claim shall be rejected and claims to the nonelected species held withdrawn from further consideration. ***The prior art search, however, will not be extended unnecessarily to cover all nonelected species.*** Should applicant, in response to this rejection of the Markush-type claim, overcome the rejection, as by amending the Markush-type claim to exclude the species anticipated or rendered obvious by the prior art, the amended Markush-type claim will be reexamined. The prior art search will be extended to the extent necessary to determine patentability of the Markush-type claim. In the event prior art is found during the reexamination that anticipates or renders obvious the amended Markush-type claim, the claim will be rejected and the action made final. Amendments submitted after the final rejection further restricting the scope of the claim may be denied entry.

Thus the search was expanded to non-elected species, which *were* found in the prior art; see rejections below.

### *Claim Objections*

11. Claims 20, 28, and 47 objected to because of the following informalities: There are typographical errors in claim 20, i.e. an apostrophe after the term "incorporated", claim 28, i.e. misspelling of "phenylboronic", and claim 47, i.e. a minus sign before the term "method".

Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 1, 3-7, 9, 11-17, 20-23, 25-26, 28, 32-34, 40-48, and 85-93 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instant claim 1 recites a method a method for identifying one or more complexes from a library of complexes. The method comprises the step of (a) preparing a library of morphatides; (b) screening the library of morphatides prepared in step (a) by contacting n g,

associating the morphatides with one or more suitable target molecules; (c) separating the morphatides performing the pre-selected or desired function or binding or associating thereby identifying one or more complexes from a library of complexes. The library of morphatides comprises (i) a scaffolding component selected from the group consisting of nucleic acid, nucleic acid like molecule or nucleic acid analog having one or regions of randomized sequence; (ii) one or more linker components; and (iii) one or more agent molecules or type of agent molecules, linked to the scaffolding component by one or more type of linker components.

The specification disclosure does not sufficiently teach the broad genus of complex or complexes, i.e. morphatides, for use in the presently claimed screening method. The broadly claimed complex or complexes, i.e. morphatides, comprises (i) a scaffolding component selected from the group consisting of nucleic acid, nucleic acid like molecule or nucleic acid analog having one or regions of randomized sequence; (ii) one or more linker components; and (iii) one or more agent molecules or type of agent molecules, linked to the scaffolding component by one or more type of linker components. The presently claimed complex or complexes lack necessary core structure for the "agent", linker, and scaffold components and the interrelationship, i.e. bonding, of these components. Additionally, the presently claimed complex or complexes has the (prospective) ability to "bind, associate or interact" to "any molecule of interest". The specification description is directed to the proverbial "laundry list" of what each of those components, i.e. the "agent", linker, and scaffold components, that would form the presently claimed complex or complexes (see e.g. specification pg. 13, lines 11-27; pg. 19, line 5 to pg. 27, line 6) and the type of 'target' to which the claimed complex or complexes has the (prospective) ability to "bind, associate or interact" (see e.g. specification pg. 27, lines 16-24). This method

clearly does not provide an adequate representation regarding the broad genus of complex or complexes, i.e. morphatides, for use in the presently claimed screening method. Thus the specification does not teach the broad genus of complex or complexes, i.e. morphatides, for use in the presently claimed screening method.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

With the exception of the "laundry list" of what each of those components, i.e. the "agent", linker, and scaffold components, that would form the presently claimed complex or complexes disclosed by the specification, the skilled artisan cannot envision the broad genus of complex or complexes, i.e. morphatides, for use in the presently claimed screening method. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

Additionally, Cf. University of Rochester v G.D. Searle & Co., Inc., Monsanto Company, Pharmacia Corporation, and Pfizer Inc., No. 03-1304, 2004 WL 260813 (Fed. Cir., Feb. 13, 2004) held that:

*Regardless whether a compound is claimed per se or a method is claimed that entails the use of the compound, the inventor cannot lay claim to that subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods.*

In the present instance, the specification does not teach the broad genus of complex or complexes, i.e. morphatides, for use in the presently claimed screening method. Therefore, the full breadth of the claim method does not meet the written description provision of 35 U.S.C 112, first paragraph.

14. Claims 1, 3-7, 9, 11-17, 20-23, 25-26, 28, 32-34, 40-48, and 85-93 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling (making/use) since there is critical or essential structure necessary to practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re* Mayhew, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976) and the claims lack metes and bounds.

There are many factors to consider when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any experimentation is "undue". These factors include, but are not limited to:

1. The breadth of the claims.
2. The nature of the invention
3. The state of the prior art;
4. The level of one of ordinary skill
5. The level of predictability in the art;
6. The amount of direction provided by the inventor;
7. The presence or absence of working examples;
8. The quantity of experimentation necessary needed to make or use the invention based on the disclosure; See :*In re Wands* USPQ 2d 1400 (CAFC 1988):

*(1-2) The breadth of the claims and the nature of the invention:*

The instant claim 1 broadly claimed the complex or complexes, i.e. library of morphatides, for use in the presently claimed screening method. The library of morphatides comprises (i) a scaffolding component selected from the group consisting of nucleic acid, nucleic acid like molecule or nucleic acid analog having one or regions of randomized sequence; (ii) one or more linker components; and (iii) one or more agent molecules or type of agent molecules, linked to the scaffolding component by one or more type of linker components. The claims further assert that the presently claimed complex or complexes has the (prospective) ability to "bind, associate or interact" to "any molecule of interest", i.e. the claimed 'scaffolding component' and 'agent component' of the complex or complexes is functionally define by functionally by its ability to "affect binding of said complex (e.g. morphatide) to a target molecule" without recitation of either degree or type of affect or recitation as to the "receptor" to

be so affected. The specification description is directed to the proverbial "laundry list" of what each of those components, i.e. the "agent", linker, and scaffold components, that would form the presently claimed complex or complexes (see e.g. specification pg. 13, lines 11-27; pg. 19, line 5 to pg. 27, line 6) and the type of 'target' to which the claimed complex or complexes has the (prospective) ability to "bind, associate or interact" (see e.g. specification pg. 27, lines 16-24). The claimed the complex or complexes, i.e. library of morphatides, thus recite incomplete compound structure, i.e. chemical relationship of scaffold, linker, and agent, necessary to elicit a single required bioactivity.

*(3 and 5) The state of the prior art and the level of predictability in the art:*

The present invention relates to a broad generic of complex or complexes (see e.g. specification pg. 13, lines 11-27; pg. 19, line 5 to pg. 27, line 6) whose utility (e.g. pharmaceutical) requires the ability of diversely structured morphatide complexes to bind (associate or interact) with various general receptor categories (see e.g. specification pg. 27, lines 16-24). The ability of the morphatide (e.g. "agent" and DNA scaffold) to efficaciously bind a given receptor is unpredictable. The unpredictability of ligand receptor binding as described in the claimed invention is known in the art. In addition, the effects, a priori, of nonconservative substitutions, which differ sterically and/or hydrophobically on substrate/ligand binding, is unpredictable; because substrate/ligand binding is stereospecitic for a nucleic acid/peptide/protein of the proper three dimensional conformational structure. Amino acid, nucleic acid, nucleic acid like molecules or nucleic acid analogs composition and the length of such chains formed from the aforementioned groups affect the three dimensional nature of a given peptide, nucleic acid, amino acid sequence, etc.

*(4) The level of one of ordinary skill in the art:*

The level of skill would be high, most likely at the Ph.D. level.

*(6-7) The amount of direction provided by the inventor and the existence of working examples.*

The broadly claims complexes which require that the complex "bind to a target molecule", i.e. act as a "ligand" and/or possess biological activity, and without reciting a specific target or a specific pharmaceutical utility, i.e. encompass binding to any target and any biological use. The specification broadly discloses that any portion or all portions of the presently claimed 'scaffolding component' and/or 'agent component' may be responsible without providing any specific examples as to a single complex. Additionally, to the extent the claims encompass nucleic acid complexes, which comprise encoding nucleic acids (e.g. the scaffold and/or the agent molecules) the specification fails to describe any nucleic acid (e.g. gene, C-DNA etc) structure, which could encode a single protein.

*(8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure:*

Both the specification and the claims lack essential compound structure (e.g. encoding nucleic acids and core agent/scaffold/linker structure). Thus, the specification provides no direction as to what nucleic acid structure or other "agent" and/or "linker" structure is needed (e.g. nonenable for using); nor does the specification provide any direction as to specific desired proteins to be encoded. Accordingly, the lack of specification direction and the lack of essential encoding nucleic acid structure and other compound structure would necessarily result in undue experimentation for one of ordinary skill wishing to practice the presently claimed invention.

Accordingly, the material composition (e.g., agents, epitope(s), etc.) of the ligand, which is critical or essential to the practice of the invention, but not included in the claim(s), is not enabled by the disclosure. See *In re* Mayhew, 527 F.2d 1229, 1 88 USPQ 356 (CCPA 1976). In this regard, it is noted that claimed the complex or complexes, i.e. library of morphatides, for use in the presently claimed screening method lack critical or essential subject matter that is necessary to the practice of the invention, but is not included in the claim(s), including essential compound structure, is not enabled by the disclosure. See *In re* Mayhew, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976); and *Ex Parte* Bhide (Bd Pat. App. & Int.) 42 USPQZd 1441.

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. Claims 1, 3-7, 9, 11-17, 20-23, 25-26, 28, 32-34, 40-48, and 85-93 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) Claim 1 recites the phrases of "nucleic acid like molecule" and "nucleic acid analog". This is vague and indefinite as it is unclear what constitutes a nucleic acid like molecule or nucleic acid derivative. Therefore, it is not possible to determine the metes and bounds of the invention as claimed.

b) Claim 86 recites the limitation "a first fixed region" in line 1 and "a second fixed region" in line 2. There is insufficient antecedent basis for this limitation in the claim 23.

c) Claim 11 recites the limitation "component(s)" in line 1. There is insufficient antecedent basis for this limitation in the claim 1.

***Claim Rejections - 35 USC § 102***

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

18. The claim 1 is interpreted as follows:

*The instant claim 1 recites a method for identifying one or more complexes from a library of complexes. The method comprises the step of (a) preparing a library of morphatides; (b) screening the library of morphatides prepared in step (a) by contacting, binding, associating the morphatides with one or more suitable target molecules; (c) separating the morphatides performing the pre-selected or desired function or binding or associating thereby identifying one or more complexes from a library of complexes. The library of morphatides comprises (i) a scaffolding component selected from the group consisting of nucleic acid, nucleic acid like molecule or nucleic acid analog having one or regions of randomized sequence; (ii) one or more linker components; and (iii) one or more agent molecules or type of agent molecules, linked to the scaffolding component by one or more type of linker components.*

19. Claims 1, 3-7, 9, 11-12, 17, 20-23, 25-26, 32-34, 40-41, and 46 are rejected under 35 U.S.C. 102(b) as being anticipated by Schatz et al. (US Patent 5,270,170).

Schatz et al. teach the screening method for identifying one or more complexes from a library of complexes (see e.g. Abstract; col. 2, lines 25-32; col. 4, lines 49-64; fig. 1 and 2). The method comprises the steps of (a) preparing a library of complexes, wherein each complex is constructed from: (i) a scaffold component with one or more regions of random nucleotide sequence (see e.g. fig. 2: Region X12; col. 3, lines 20-34); (ii) at least one linker component comprised of a protein (lac I) and a nucleotide (the Lac O sequences), or alternatively a linker comprised of the lac I proteins; (iii) an agent molecule (the random peptide associated with Lac 1, encoded by the random oligonucleotide, X12 and also encode a binding site for a DNA binding protein, which can be used to screen for novel ligands); and once a peptide ligand of interest has been identified, a variety of techniques can be used to diversify a peptide library to construct ligands with improved properties, including the use of the polymerase chain reaction, i.e. PCR, techniques, mutagenesis of a pool or recovered set of peptide vectors, and a variety of methods for adding additional amino acids to a peptide or peptides found to be active (see, col. 15, lines 1-4, 19-23, 27-29 and 42-45; and (b) a method for screening the aforementioned library complexes to identify peptides that bind to receptor molecules of interest or gene products that modify peptides or RNA in a desired fashion (see, col. 4, lines 49-64): (a) through binding or contacting of such complexes with target or receptor molecules (see e.g. fig. 3); (b) to identify ligands for receptors, carbohydrates non-protein organic compounds or as a diagnostic reagent which reads on identifying the presence of a target substance in a sample (see, col. 25, lines 25-42) and (c) isolation or separation of the complexes (for example, a nucleic acid can be isolated from a vector that encodes a peptide that binds to said receptor, which can then be sequenced to

determine the amino sequence of the desired peptide; see, col. 2, lines 57-59 and col. 4, lines 59-61). Thus the method of Schatz et al. anticipates the presently claimed method.

20. Claims 1, 3-7, and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Lam et al. (US Patent 5,510,240).

Lam et al. discloses a method for determining the sequence if a bio-oligomer ligand for an acceptor molecule (see e.g. Abstract; col. 4, lines 65 to col. 5, line 42) comprising the steps of (a) generating a random biooligomer complex or a corresponding library (i.e., a library is a composition comprised of two or more components), which include nucleic acids, peptides, oligonucleotide, peptide oligonucleotide chimeras or combinations therein (see e.g. col. 6, line 65 to col. 7, line 5) attached to solid supports; wherein the peptide portion of those biooligomers can act as an agent molecules; the nucleotide or amino acid joining the chimera is the linker; and the oligonucleotide forms the scaffold (see e.g. col. 6, line 65 to col. 7, line 5; col. 14, line 50 to col. 15, line 37); (b) introducing to such a random library, an acceptor molecule, for screening purposes to recognize and bind one ore more solid phase support/oligomer species within the library to (a) identify and characterize ligands capable of binding an acceptor molecule, (b) mediating a biological activity of interest or (c) catalyze a chemical reaction; (c) isolating a solid phase support/bio-oligomer combination that exhibits the desired property; (d) sequencing the bio-oligomer of the isolated solid phase support/bio-oligomer; (e) the bio-oligomer is separated or released from the solid phase support/bio-oligomer combination in situ and a biological activity is detected in situ (see e.g. col. 5, lines 19-42; col. 17, line 5 to col. 28, line 39). Therefore, the method of Lam et al. anticipates the presently claimed method.

21. Claims 1, 3, 5-7, 9, 12, 21, 23, 25, 32-34, 40-43, 46 and 85 are rejected under 35 U.S.C. 102(e) as being anticipated by Biesecker et al. (US Patent 5,683,867).

Biesecker et al. teaches a method for identifying a complex from a library of complexes for their ability to perform a desired function on a target molecule (see e.g. Abstract; col. 1, lines 63-67; col. 2, lines 9-26, and 41-59). The method comprises the step of 1) preparing a candidate mixture of nucleic acids of different sequences (refers to the claimed scaffolding component), wherein the nucleic acid includes regions of fixed sequences and regions of randomized sequences (refers to the presently claimed preparation step); 2) contacting the candidate mixture of nucleic acids with a target (refers to the presently claimed screening step); 3) partitioning those nucleic acids with the highest affinity for the target from the nucleic acids with the lesser affinity (refers to the presently claimed separating step); and 4) amplified those nucleic acids nucleic acid during the partitioning step (see e.g. col. 2, lines 9-26, and 41-59; col. 6, lines 14-62). The candidate mixture of nucleic acids include blended nucleic acid ligand wherein functional unit(s) (refers to the claimed agent component) such as peptides are coupled to the nucleotides (see e.g. Abstract; col. 1, lines 25-50; col. 4, lines 43-51; col. 7, lines 6-17, and 44-60). Additionally, coupling the functional unit(s) to the nucleotides comprises a linker (refers to the claimed linker component) (see e.g. fig. 1, and 7) and the site of attachment includes an individual nucleic acid residue such as derivatized uridine base (see col. 7, lines 44-60; col. 8, lines 7-26; fig. 1). The functional unit(s) can be dissociated from the nucleic acid sequences after the partitioning step in order for the amplification step (see e.g. col. 10, lines 33-65). Thus the method of Biesecker et al. anticipates the presently claimed method.

***Claim Rejections - 35 USC § 103***

22. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

23. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

24. The claim 1 is interpreted as follows:

*The instant claim 1 recites a method for identifying one or more complexes from a library of complexes. The method comprises the step of (a) preparing a library of morphatides; (b) screening the library of morphatides prepared in step (a) by contacting n g, associating the morphatides with one or more suitable target molecules; (c) separating the morphatides performing the pre-selected or desired function or binding or associating thereby identifying one or more complexes from a library of complexes. The library of morphatides comprises (i) a scaffolding component selected from the group consisting of nucleic acid, nucleic acid like molecule or nucleic acid analog having one or regions of randomized sequence; (ii) one or more linker components; and (iii) one or more agent molecules or type of agent molecules, linked to the scaffolding component by one or more type of linker components.*

25. Claims 1, 3, 5-7, 9, 12, 21, 28, 32-34, 40-43, 46, 85 and 87-89 are rejected under 35 U.S.C. 103(a) as being unpatentable over Biesecker et al. (US Patent 5,683,867) and Stolowitz et al. (US Patent 5,847,192).

Biesecker et al. teaches a method for identifying a complex from a library of complexes for their ability to perform a desired function on a target molecule (see e.g. Abstract; col. 1, lines 63-67; col. 2, lines 9-26, and 41-59). The method comprises the step of 1) preparing a candidate mixture of nucleic acids of different sequences (refers to the claimed scaffolding component), wherein the nucleic acid includes regions of fixed sequences and regions of randomized sequences (refers to the presently claimed preparation step); 2) contacting the candidate mixture of nucleic acids with a target (refers to the presently claimed screening step); 3) partitioning those nucleic acids with the highest affinity for the target from the nucleic acids with the lesser affinity (refers to the presently claimed separating step); and 4) amplified those nucleic acids nucleic acid during the partitioning step (see e.g. col. 2, lines 9-26, and 41-59; col. 6, lines 14-62). The candidate mixture of nucleic acids include blended nucleic acid ligand wherein functional unit(s) (refers to the claimed agent component) such as peptides are coupled to the nucleotides (see e.g. Abstract; col. 1, lines 25-50; col. 4, lines 43-51; col. 7, lines 6-17, and 44-60). Additionally, coupling the functional unit(s) to the nucleotides comprises a linker (refers to the claimed linker component) (see e.g. fig. 1, and 7) and the site of attachment includes an individual nucleic acid residue such as derivatized uridine base (see col. 7, lines 44-60; col. 8, lines 7-26; fig. 1). The functional unit(s) can be dissociated from the nucleic acid sequences after the partitioning step in order for the amplification step (see e.g. col. 10, lines 33-65).

The method of Biesecker et al. differs from the presently claimed invention by failing to include the linker that is a phenylboronic acid linker.

Stolowitz et al. teaches the method conjugating biological macromolecules such as protein, and nucleic acid with each other to form a bioconjugates (see e.g. Abstract; col. 1, lines 13-40; col. 3, line 66 to col. 4, line 27). The conjugation is an indirect conjugation using a linker such as a phenylboronic acid linker (see e.g. col. 3, line 66 to col. 4, line 27; col. 5, line 46 to col. 6, line 20).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include a phenylboronic acid linker as taught by Stolowitz et al. in the method of Biesecker et al. One of ordinary skill in the art would have been motivated to include a phenylboronic acid linker in the method of Biesecker et al. for the advantage of providing a linker that is known to react with a wide range of polar molecules and forming complexes with varying stability (Stolowitz: col. 2, lines 41-47) since both Biesecker et al. and Stolowitz et al. disclose bioconjugate comprising nucleic acid and protein (Biesecker: col. 1, lines 25-50; col. 4, lines 43-51; Stolowitz: col. 1, lines 13-40; col. 3, line 66 to col. 4, line 27). Furthermore, one of ordinary skill in the art would have reasonably expectation of success in the combination of Biesecker et al. and Stolowitz et al. because Stolowitz et al. has exemplified the bioconjugates of nucleic acid and protein with a phenylboronic acid linker (see e.g. col. 29, example XIII; col. 31, examples XIII and XIV).

26. Claims 1, 3-7, 9, 11-17, 21, 32-34, 40-43, 46 and 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Biesecker et al. (US Patent 5,683,867) and Bock et al. (*Nature*, **1992**, 355(6360):564-566).

Biesecker et al. teaches a method for identifying a complex from a library of complexes for their ability to perform a desired function on a target molecule (see e.g. Abstract; col. 1, lines 63-67; col. 2, lines 9-26, and 41-59). The method comprises the step of 1) preparing a candidate mixture of nucleic acids of different sequences (refers to the claimed scaffolding component), wherein the nucleic acid includes regions of fixed sequences and regions of randomized sequences (refers to the presently claimed preparation step); 2) contacting the candidate mixture of nucleic acids with a target (refers to the presently claimed screening step); 3) partitioning those nucleic acids with the highest affinity for the target from the nucleic acids with the lesser affinity (refers to the presently claimed separating step); and 4) amplified those nucleic acids nucleic acid during the partitioning step (see e.g. col. 2, lines 9-26, and 41-59; col. 6, lines 14-62). The candidate mixture of nucleic acids include blended nucleic acid ligand wherein functional unit(s) (refers to the claimed agent component) such as peptides are coupled to the nucleotides (see e.g. Abstract; col. 1, lines 25-50; col. 4, lines 43-51; col. 7, lines 6-17, and 44-60). Additionally, coupling the functional unit(s) to the nucleotides comprises a linker (refers to the claimed linker component) (see e.g. fig. 1, and 7) and the site of attachment includes an individual nucleic acid residue such as derivatized uridine base (see col. 7, lines 44-60; col. 8, lines 7-26; fig. 1). The functional unit(s) can be dissociated from the nucleic acid sequences after the partitioning step in order for the amplification step (see e.g. col. 10, lines 33-65).

The method of Biesecker et al. differs from the presently claimed invention by failing to include the target that is bound to a solid support and the region of randomized sequence is between two regions of fixed sequence.

Bock et al. teaches the method of selecting single-stranded DNA molecules that bind and inhibit human thrombin (see e.g. Abstract; pg. 564, lines 1-13; pg. 565, fig. 1). The method comprises the steps of 1) synthesizing a pool of oligomers wherein each oligomer comprises the region of randomized sequence is between two regions of fixed sequence; 2) the pool of oligomers are reacted with agarose immobilized thrombin; and 3) the thrombin-DNA complexes are separated and identified (see e.g. pg. 564, right col., lines 1-13; pg. 565, fig. 1; pg. 566, left col., line 19-21).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include the target that is bound to a solid support and the region of randomized sequence is between two regions of fixed sequence as taught by Bock et al. in the method of Biesecker et al. One of ordinary skill in the art would have been motivated to include the target that is bound to a solid support and the region of randomized sequence is between two regions of fixed sequence in the method of Biesecker et al. because the type of target, i.e. support bound target, and the positioning of the region of randomized sequence, i.e. between two regions of fixed sequence, would be a choice of experimental design and is considered within the purview of the cited prior art. Furthermore, one of ordinary skill in the art would have reasonably expectation of success in the combination of Biesecker et al. and Bock et al. because Bock et al. has exemplified the method of selecting DNA complexes that perform a desired function on a target molecule wherein the DNA complexes comprises a region of randomized

sequence is between two regions of fixed sequence and the target that is bound to a solid support (Bock: pg. 566, right col., lines 16-35; pg. 566 fig. 2).

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MY-CHAU T TRAN whose telephone number is 571-272-0810. The examiner can normally be reached on Mon.: 8:00-2:30; Tues.-Thurs.: 7:30-5:00; Fri.: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANDREW WANG can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

mct
October 22, 2004

PADMASHRI PONNALURI
PRIMARY EXAMINER